IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appln. No. : 10/010,114 Confirmation No. 5743

Applicant : Raymond H. Boutin

Filed : November 13, 2001

TC/A.U : 1632

Examiner : D. Crouch

Docket No. : AHP1CUSA

Customer No. 38199

Mail Stop PETITION
Commissioner for Patents
Post Office Box 1450
Alexandria, VA 22313-1450

PETITION PURSUANT TO 37 CFR 1.78(a)(3)

Sir:

Applicant respectfully requests that the reference required by 35 USC 120 and 37 CFR 1.78(a)(2) to a prior-filed co-pending nonprovisional application on international application designating the United States of America be accepted pursuant to the provisions of 37 CFR 1.78(a)(3).

The reference required by 35 USC 120 and paragraph 37 CFR 1.78(a)(2) has been previously submitted, a check for the surcharge is enclosed, and applicant states that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2)(ii) of this section and the date the claim was filed was unintentional. The facts are as follows.

Applicant attaches a copy of a request to correct the filing receipt issued the present application. The filing receipt lists domestic priority claims to US Patent Application No. 09/425,595 (the parent of this application, US Patent Application No. 09/809,397 (the grand-parent of this application), and PCT/US95/12502 (of which the

Express Mail No. EU531574436US

grandparent application was a national stage application). However, the filing receipt omitted the US application from which the PCT application claims priority, US Patent Application No. 08/314,060, filed September 28, 1998, now US Patent 5,837,533.

Preliminary Amendment A, filed with the application on November 12, 2001, inserted a cross-reference to related applications, which identified all of these priority documents, including the original priority application, which the PCT application was stated to 'claim the benefit of the priority thereof". Applicant filed a Request for Correction of Filing Receipt on March 19, 2002, but no reply was received.

Applicant filed a second Request for Correction of Filing Receipt on May 22, 2002, together with Preliminary Amendment B, in which the status of the parent application was updated and the PCT application was stated to be "a continuation-in-part of US Patent Application No. 08/314,060". No reply to this Request was received.

In the course of preparing a response to the Office Action dated December 8, 2003, Applicant noted that no corrected Filing Receipt had been issued and therefore submits this Petition.

Applicant believes that amendment filed May 22, 2002 corrected the priority claim under 35 USC 120, 121 or 365(c).

The entire delay between the date the claim was due under 37 CFR 1.78(a)(2)(ii) and the date the claim was filed was unintentional.

Applicant and the undersigned respectfully request that the unintentionally delayed claim to the application of which the international application is a continuation-in-part be granted. The undersigned invites the Director, or his representative, to telephone if additional information is required.

A check in the amount of the surcharge, $1330, is enclosed herewith.

The Director of the US Patent and Trademark Office is hereby authorized to charge any other fees due with the filing of this paper, or any credit, to Deposit Account No. 08-3040.

Respectfully submitted,
HOWSON AND HOWSON
Attorneys for Applicant

By Cathy A Kodroff

Cathy A. Kodroff
Registration No. 33,980
Spring House Corporate Center
Box 457
Spring House, PA 19477
Telephone: (215) 540-9210
Telefacsimile: (215) 540-5818

AHP1CUSA

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of	) Group Art Unit: 1632
Raymond H. Boutin	) Examiner:
Appln. No. 10/010,114	)
Filed: November 13, 2001	)
For: MULTIFUNCTIONAL MOLECULAR COMPLEXES FOR GENE TRANSFER TO CELLS	) March 19, 2002

Assistant Commissioner for Patents
Washington, DC 20231

ATTN: OIPE - Customer Service Center

REQUEST FOR CORRECTION OF FILING RECEIPT

Sir:

Enclosed is a copy of the Filing Receipt received in the above-identified patent application. Errors in the Domestic Priority Data information for this application have been noted and correction to same is marked in red on the attached copy of the Filing Receipt (Exhibit A). A copy of the first page of the Preliminary Amendment filed on November 13, 2001 as well as the first page of Appendix A - Version with Markings to Show Changes Made (Exhibits B and C) are attached to show the correct domestic priority data information.

Applicants respectfully request that the official filing receipt for this application be corrected to reflect the correct priority data to which Applicants are entitled.

CERTIFICATE UNDER 37 CFR §1.8(a)

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: the Assistant Commissioner for Patents, Washington, DC 20231 on March 19, 2002.

Signature _____

Typed or printed name Debra N. Gerstemeier

The Director of the U. S. Patent and Trademark Office is hereby authorized to charge any deficiency in any fees due with the filing of this paper or credit any overpayment in any fees paid on the filing, or during prosecution of this application to Deposit Account No. 08-3040.

Respectfully submitted,

HOWSON AND HOWSON
Attorneys for the Applicants

By _____

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Telephone: (215) 540-9210
Telefacsimile: (215) 540-5818

UNITED STATES PATENT AND TRADEMARK OFFICE

COMMISSIONER FOR PATENTS
UNITED STATES PATENT AND TRADEMARK OFFICE
WASHINGTON, D.C. 20231
www.uspto.gov

APPLICATION NUMBER	FILING DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	DRAWINGS	TOT CLAIMS	IND CLAIMS
10/010,114	11/13/2001	1632	1244	AHP1CUSA		48	3

CONFIRMATION NO. 5743

00270
HOWSON AND HOWSON
ONE SPRING HOUSE CORPORATION CENTER
BOX 457
321 NORRISTOWN ROAD
SPRING HOUSE, PA 19477

FILING RECEIPT

OC000000007491386

Date Mailed: 02/19/2002

Receipt is acknowledged of this nonprovisional Patent Application. It will be considered in its order and you will be notified as to the results of the examination. Be sure to provide the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION when inquiring about this application. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please write to the Office of Initial Patent Examination's Customer Service Center. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections (if appropriate).**

Applicant(s)

Raymond H. Boutin, Thornton, PA;

Assignment For Published Patent Application

American Home Products Corporation, Madison, NJ;

Domestic Priority data as claimed by applicant

THIS APPLICATION IS A DIV OF 09/425,597 10/22/1999
WHICH IS A DIV OF 08/809,397 03/21/1997 PAT 6,127,170
WHICH IS A 371 OF PCT/US95/12502 09/28/1995
WHICH CLAIMS THE BENEFIT OF 08/314,040 09/28/1994 PAT 5,837,53

Foreign Applications

If Required, Foreign Filing License Granted 02/15/2002

Projected Publication Date: 05/30/2002

Non-Publication Request: No

Early Publication Request: No

Title

Exhibit A

AHP1CUSA

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of	) Group Art Unit: 1632
Raymond H. Boutin	) Examiner: D. Crouch
Appln. No.	)
Filed: Herewith	)
For: MULTIFUNCTIONAL MOLECULAR COMPLEXES FOR GENE TRANSFER TO CELLS	) November 13, 2001

Assistant Commissioner for Patents
Box Sequence
Washington, DC 20231

PRELIMINARY AMENDMENT A

Sir:

Please amend the above-identified patent application as follows.

In the Specification

Page 1, line 3, before "Background of the Invention", insert the following new paragraph:

-- CROSS-REFERENCE TO RELATED APPLICATIONS

This is a divisional of U. S. Patent Application No. 09/425,597, filed October 22, 1999, which is a divisional of U. S. Patent Application No. 08/809,397, filed March 21, 1997, now U. S. Patent No. 6,127,170, issued October 3, 2000, which is a 35 USC §371 of PCT/US95/12502, filed September 28, 1995, which claims the benefit of the priority of U. S. Patent Application No. 08/314,060, filed September 28, 1994, now U. S. Patent No. 5,837,533, issued November 17, 1998. --

Express Mail No. ET033435671US

Exhibit B

Appendix A

Version with Markings to Show Changes Made

In the specification:

Page 1, line 3, before "Background of the Invention", insert the following new paragraph:

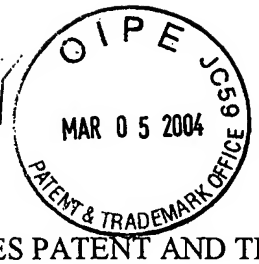
-- CROSS-REFERENCE TO RELATED APPLICATIONS

This is a divisional of U. S. Patent Application No. 09/425,597, filed October 22, 1999, which is a divisional of U. S. Patent Application No. 08/809,397, filed March 21, 1997, now U. S. Patent No. 6,127,170, issued October 3, 2000, which is a 35 USC §371 of PCT/US95/12502, filed September 28, 1995, which claims the benefit of the priority of U. S. Patent Application No. 08/314,060, filed September 28, 1994, now U. S. Patent No. 5,837,533, issued November 17, 1998. --

Page 11, delete the paragraph spanning lines 1-9 and replace it with the following paragraph:

-- Combinations of lipids have been used to facilitate the transfer of nucleic acids into cells. For example, in US Patent 5,283,185 there is disclosed such a method which utilizes a mixed lipid dispersion of a cationic lipid with a co-lipid in a suitable solvent. The lipid has a structure which includes a lipophilic group derived from ~~chlolesterol~~ cholesterol, a linker bond, a linear alkyl spacer arm, and a cationic amino group; and the co-lipid is phosphatidylcholine or phosphatidylethanolamine. --

Exhibit C



00270
PATENT TRADEMARK OFFICE

AHP1CUSA

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of	) Group Art Unit: 1632
Raymond H. Boutin	) Examiner:
Appln. No. 10/010,114	)
Filed: November 13, 2001	)
For: MULTIFUNCTIONAL MOLECULAR COMPLEXES FOR GENE TRANSFER TO CELLS	) May 9, 2002

Assistant Commissioner for Patents
Office of Initial Patent Examination
Customer Service Center
Washington, DC 20231

REQUEST FOR CORRECTION OF FILING RECEIPT

Sir:

Pursuant to Applicant's previous Request for Correction of Filing Receipt filed March 27, 2002, Applicant and the undersigned attorney herewith submit a corrected Request for Correction of Filing Receipt indicating the correct relationship in the continuity claimed under 35 USC 120 as marked in red on the attached copy of the Filing Receipt (Exhibit A).

Applicant respectfully requests that the official filing receipt for this application be corrected to reflect the priority data to which Applicant is entitled.

CERTIFICATE UNDER 37 CFR §1.8(a)

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: the Assistant Commissioner for Patents, Washington, DC 20231 on May 9, 2002.

Signature _____

Typed or printed name Debra N. Gerstemeier

The Director of the U. S. Patent and Trademark Office is hereby authorized to charge any deficiency in any fees due with the filing of this paper or credit any overpayment in any fees paid on the filing, or during prosecution of this application to Deposit Account No. 08-3040.

Respectfully submitted,

HOWSON AND HOWSON
Attorneys for the Applicants

By _____

Cathy A. Kodroff
Registration No. 33,980
Spring House Corporate Center
Box 457
Spring House, PA 19477
Telephone: (215) 540-9210
Telefacsimile: (215) 540-5818

UNITED STATES PATENT AND TRADEMARK OFFICE

COMMISSIONER FOR PATENTS
UNITED STATES PATENT AND TRADEMARK OFFICE
WASHINGTON, D.C. 20231
www.uspto.gov

APPLICATION NUMBER	FILING DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	DRAWINGS	TOT CLAIMS	IND CLAIMS
10/010,114	11/13/2001	1632	1244	AHP1CUSA		48	3

CONFIRMATION NO. 5743

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BOX 457
321 NORRISTOWN ROAD
SPRING HOUSE, PA 19477

FILING RECEIPT

OC000000007491386

Date Mailed: 02/19/2002

Receipt is acknowledged of this nonprovisional Patent Application. It will be considered in its order and you will be notified as to the results of the examination. Be sure to provide the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION when inquiring about this application. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please write to the Office of Initial Patent Examination's Customer Service Center. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections (if appropriate).**

Applicant(s)

Raymond H. Boutin, Thornton, PA;

Assignment For Published Patent Application

American Home Products Corporation, Madison, NJ;

Domestic Priority data as claimed by applicant

THIS APPLICATION IS A DIV OF 09/425,597 10/22/1999, PAT 6,379,965
WHICH IS A DIV OF 08/809,397 03/21/1997 PAT 6,127,170
WHICH IS A 371 OF PCT/US95/12502 09/28/1995
WHICH IS A CIP OF 08/314,060 09/28/1994 PAT 5,837,533

Foreign Applications

If Required, Foreign Filing License Granted 02/15/2002

Projected Publication Date: 05/30/2002

Non-Publication Request: No

Early Publication Request: No

Title

Exhibit A

COPY

PATENT

Serial No. 10/010114 Doc. No. AHPICV-3A Atty/Sec OAK/cb

Inventor Raymond H. Boston Client AHP Date 5-9-2002

Title Multifunctional Molecular Complexes for Gene Transfer to Cells

The following has been received in the U.S. Patent and Trademark Office on the date stamped hereon:

___ ___ pp. Spec., ___ Claims, ___ Abstract
___ ___ pp. Declaration/Power of Attorney
___ ___ pp. Verified Statement (Small Entry)
___ ___ shts. Informal Drawings
___ ___ shts. Formal Drawings
___ ___ pp. Assignment
✓ 2 pp. Preliminary Amendment
___ ___ pp. Extension of Time
___ ___ pp. Information Disclosure Statement with PTO-1449 and ___ references

___ ___ pp. Amendment: OA dtd ___
___ ___ pp. Response: OA dtd ___
✓ 1 pp. Transmittal Letter
___ Issue Fee
___ Notice of Appeal & Fee
___ Check # ___ for $ ___
✓ 1pg Appendix A-Version w/ Markings to Show Changes Made.

The Patent and Trademark Office is respectfully requested to place its stamp on this postal card and place it in the outgoing mail.

Respectfully,
HOWSON AND HOWSON
OAK

00270

PTO/SB/21 (08-00)
Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	10/010,114
Filing Date	11/13/2001
First Named Inventor	Raymond H. Boutin
Group Art Unit	1632
Examiner Name	
Total Number of Pages in This Submission: 4	Attorney Docket Number: AHP1CUSA

ENCLOSURES *(check all that apply)*

- ☐ Fee Transmittal Form
  - ☐ Fee Attached
- ☑ Amendment / Reply
  - ☐ After Final
  - ☐ Affidavits/declaration(s)
- ☐ Extension of Time Request
- ☐ Express Abandonment Request
- ☐ Information Disclosure Statement
- ☐ Certified Copy of Priority Document(s)
- ☐ Response to Missing Parts/ Incomplete Application
  - ☐ Response to Missing Parts under 37 CFR 1.52 or 1.53
- ☐ Assignment Papers *(for an Application)*
- ☐ Drawing(s)
- ☐ Licensing-related Papers
- ☐ Petition
- ☐ Petition to Convert to a Provisional Application
- ☐ Power of Attorney, Revocation Change of Correspondence Address
- ☐ Terminal Disclaimer
- ☐ Request for Refund
- ☐ CD, Number of CD(s) _____
- ☐ After Allowance Communication to Group
- ☐ Appeal Communication to Board of Appeals and Interferences
- ☐ Appeal Communication to Group *(Appeal Notice, Brief, Reply Brief)*
- ☐ Proprietary Information
- ☐ Status Letter
- ☐ Other Enclosure(s) *(please identify below)*:

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual name	Cathy A. Kodroff, Esquire Howson and Howson
Signature	Cathy A Kodroff
Date	5-9-2002

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, Washington, DC 20231 on this date: 05/09/2002

Typed or printed name	Debra N. Gerstemeier		
Signature		Date	5-9-2002

Burden Hour Statement: This form is estimated to take 0.2 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

AHP1CUSA

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of	) Group Art Unit: 1632
Raymond H. Boutin	) Examiner:
Appln. No.: 10/010,114	)
Filed: November 13, 2001	)
For: MULTIFUNCTIONAL MOLECULAR COMPLEXES FOR GENE TRANSFER TO CELLS	) May 9, 2002

Assistant Commissioner for Patents
Washington, DC 20231

PRELIMINARY AMENDMENT B

Sir:

Please enter the following amendment to the specification as set forth below.

In the Specification

Page 1, line 3, before "Background of the Invention", kindly replace the "Cross-Reference to Related Applications" paragraph added in the amendment of November 13, 2001, to read as follows:

-- CROSS-REFERENCE TO RELATED APPLICATIONS

This is a divisional of U. S. Patent Application No. 09/425,597, filed October 22, 1999, now U. S. Patent No. 6,379,965, issued April 30, 2002, which is a divisional of U. S. Patent Application No. 08/809,397, filed March 21, 1997, now U. S. Patent No. 6,127,170, issued October 3, 2000, which is a 371 of PCT/US95/12502, filed September 28, 1995, which is a continuation-in-part of U. S. Patent Application No. 08/314,060, filed September 28, 1994, now U. S. Patent No. 5,837,533, issued November 17, 1998. --

CERTIFICATE UNDER 37 CFR §1.8(a)

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: the Assistant Commissioner for Patents, Washington, DC 20231 on May 9, 2002.

Signature _____

Typed or printed name Debra N. Gerstemeier

REMARKS

The above amendment to the specification is made to update the cross-reference to related applications. No new matter is added by this amendment.

Attached hereto is a marked-up version of the changes made to the specification by the current amendment. The attached Appendix A is captioned "**Version With Markings to Show Changes Made**".

The Director of the U. S. Patent and Trademark Office is hereby authorized to charge any deficiency in any fees due with the filing of this paper or credit any overpayment in any fees to our Deposit Account No. 08-3040.

Respectfully submitted,

HOWSON AND HOWSON
Attorneys for the Applicants

By _____

Cathy A. Kodroff
Registration No. 33,980
Spring House Corporate Center
Box 457
Spring House, PA 19477
Telephone: (215) 540-9210
Telefacsimile: (215) 540-5818

Appendix A

Version with Markings to Show Changes Made

In the specification:

Page 1, line 3, before "Background of the Invention", kindly replace the "Cross-Reference to Related Applications" paragraph added in the amendment of November 13, 2001, to read as follows:

CROSS-REFERENCE TO RELATED APPLICATIONS

This is a divisional of U. S. Patent Application No. 09/425,597, filed October 22, 1999, now U. S. Patent No. 6,379,965, issued April 30, 2002, which is a divisional of U. S. Patent Application No. 08/809,397, filed March 21, 1997, now U. S. Patent No. 6,127,170, issued October 3, 2000, which is a 371 of PCT/US95/12502, filed September 28, 1995, which is a continuation-in-part of U. S. Patent Application No. 08/314,060, filed September 28, 1994, now U. S. Patent No. 5,837,533, issued November 17, 1998.

AHP1AUSA

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of	) Group Art Unit: 1632
Raymond H. Boutin	)
Appln No. 08/809,397	) Examiner: D. Crouch
Filed: March 21, 1997	)
For: MULTIFUNCTIONAL MOLECULAR COMPLEXES FOR GENE TRANSFER TO CELLS	) November 20, 1998

Asst. Commissioner for Patents
Washington, DC 20231

DECLARATION PURSUANT TO 37 CFR 1.132

Sir:

I, Julia Schauer, residing at 140 Swinehart Road, Coatesville, Pennsylvania 19320, a citizen of the United States of America, do declare and state that:

1. I am employed by assignee of the above-identified patent application and I am a member of the project team responsible for the subject matter of this application.

CERTIFICATE UNDER 37 CFR 1.8(a)

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail on the date indicated below in an envelope addressed to: Assistant Commissioner for Patents, Washington, DC 20231.

Signature _____

Date 1-12-99

2. My educational background includes a bachelor of science in Chemistry and additional pre-medical course work. I have had fourteen years of experience in the field of drug design and vaccine development and I am currently so employed. A copy of my résumé is attached.

3. I have read and understood the specification of this application.

4. I understand that the data provided herein is being presented to provide additional evidence to support the utility of the pharmaceutical compositions of the invention. The experiments described herein were performed or coordinated by me.

5. The experiment described in Paragraphs 6 and 7 below were performed to determine the ability of the multifunctional molecular complexes of the invention to transfer nucleic acids. The data demonstrates that several different multifunctional molecular complexes according to claim 1 enhance expression of plasmid DNA gene products in cultured cells as compared to control cells which were treated with DNA alone.

6. Four exemplary multifunctional molecular complexes according to claim 1, containing DNA and a transfer moiety selected from bis-octyl-bis-guanidino spermine, cholesteryl spermidine, benzyldodecyl spermidine, or cholesterol spermine were prepared as described in the specification. Briefly, plasmid DNA (2 μg) coding for the luciferase enzyme was mixed with the transfer moieties identified above at various ratios and allowed to form multifunctional molecular complexes according to claim 1. These complexes, as well as naked DNA, were applied to human rhabdomyosarcoma (RD) cells at approximately 80% confluency. After 4 hours, the cells were washed, given fresh media and incubated for up to 48 hours. The cells were lysed, and the gene product was measured by a standard luciferase assay.

7. The results are illustrated in Exhibits 1 through 4, attached. As is readily apparent from these Exhibits, transfection of human RD cells by DNA complexed in each of the exemplary transfer moieties of the invention was enhanced, as compared to transfection of the cells by DNA alone.

8. Thus, the experiments presented in Paragraphs 6 and 7 demonstrate that a variety of different multifunctional molecular complexes of the invention enhance the expression of plasmid DNA gene product in cultured cells over cells treated with DNA alone.

9. In a series of experiments similar to those described in Paragraph 6, multifunctional molecular complexes of the invention containing DNA complexed with cholesteryl spermine or cholesteryl spermidine, have been demonstrated to mediate transfection of a variety of cell types *in vitro*. Although performance varied by cell type, use of the multifunctional molecular complexes of the invention resulted in the transfer of complexed DNA in cell types including, among others, human rhabdomyosarcoma (RD), human hepatocellular carcinoma (HUH 7), human hepatocytes (FOCUS), human hepatoblastoma (HEP 2), mouse embryo (NIH/3T2), human colon carcinoma (LS 180), SV40 transformed monkey kidney (COS-1), human osteosarcoma (U-2 OS), adenovirus-transformed human kidney cells (293), human breast cancer (MCF7), human neuronal blastoma (SY5Y), and primary human hepatocytes. These experiments demonstrated the utility of the multifunctional molecular complexes of the invention in mediating transfer of DNA in a wide variety of cell types.

10. The experiment described in Paragraphs 11 - 15 demonstrate the ability of the pharmaceutical compositions of the invention to induce immune responses *in vivo*.

11. A multifunctional molecular complex of the invention, containing 50 μg plasmid DNA coding for the gD protein of herpes simplex virus type 2 (HSV-2) and transfer moiety cholesteryl spermine (CSm), was prepared as described in the specification. An equivalent amount of plasmid DNA (50 μg) was (a) uncomplexed and thus administered as naked DNA or (b) complexed with 0.25% bupivacaine. To form a pharmaceutical composition of the invention, the multifunctional molecular complex of the invention was formulated with 20% v/v polyethylene glycol 300 USP/NF in water. The naked DNA and the DNA complexed with bupivacaine were similarly formulated. The pharmaceutical composition of the invention, the naked DNA, and the DNA complexed with bupivacaine were each administered intramuscularly (im) as a single dose to mice. The cellular and humoral immune responses against gD were measured after 30 days as described in Paragraphs 12 and 13.

12. Cellular responses were measured by carrying out a lympho-proliferation assay on spleen cells of mice that received the compositions described in Paragraph 11. For the pharmaceutical compositions containing the multifunctional molecular complex of the invention, the charge ratios of transfer moiety to DNA were varied between 0.7:1, 1.0:1, and 1.5:1. The spleen cells were cultured with or without antigen, and the counts were recorded as delta counts per million [DCPM]. The results are illustrated in Exhibit 5, attached.

13. Humoral responses were measured by carrying out a standard ELISA assay on the serum samples obtained from mice that received the compositions described in Paragraph 11. For the pharmaceutical compositions containing the multifunctional molecular complex of the invention, the charge ratios of transfer moiety to DNA were varied between 0.7:1, 1.0:1, and 1.5:1. The quantitative measure of antigen specific antibody is expressed as optical density at 450 nm (OD_{450}). These results are illustrated in Exhibit 6, attached.

14. Following one intramuscular injection of a pharmaceutical composition of the invention, both cellular and humoral immune responses were measured. This experiment shows that mice that received 0.7:1 ratio of CSm:DNA had higher cellular (Exhibit 5) and humoral (Exhibit 6) responses compared to animals receiving naked DNA, DNA complexed with bupivacaine or DNA complexed with the transfer moieties at ratios of 1.0:1 and 1.5:1. Because this was a first-round experiment, the results are non-optimal, yet the ability of the pharmaceutical compositions of the invention to induce an immune response is clearly demonstrated. Further, the ability of the pharmaceutical compositions of the invention to enhance the immune response over naked DNA is evident.

15. The *in vivo* experimental data presented in Paragraphs 10 to 14 correlates with the experimental evidence described in Paragraph 9, which demonstrates the ability of the multifunctional molecular complexes of the invention to mediate transfection of a variety of cell types. Thus, the data provided herein supports the ability of the pharmaceutical compositions of the invention to successfully transfer DNA to host cells and that the DNA is expressed in a manner which elicits an immune response.

16. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: 11-24-98

By: Julia Schauer

Julia Schauer

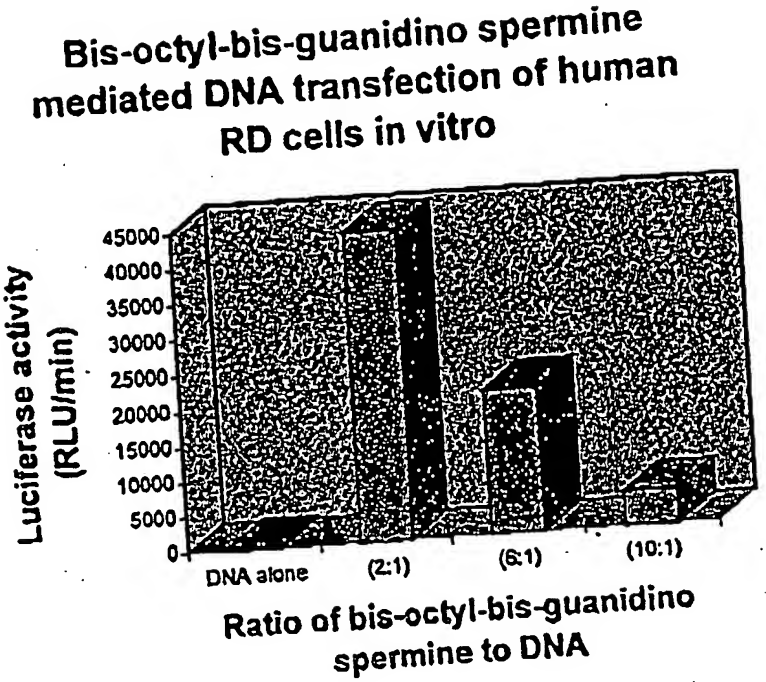

Exhibit 1
Rule 132 Declaration
08/809,397

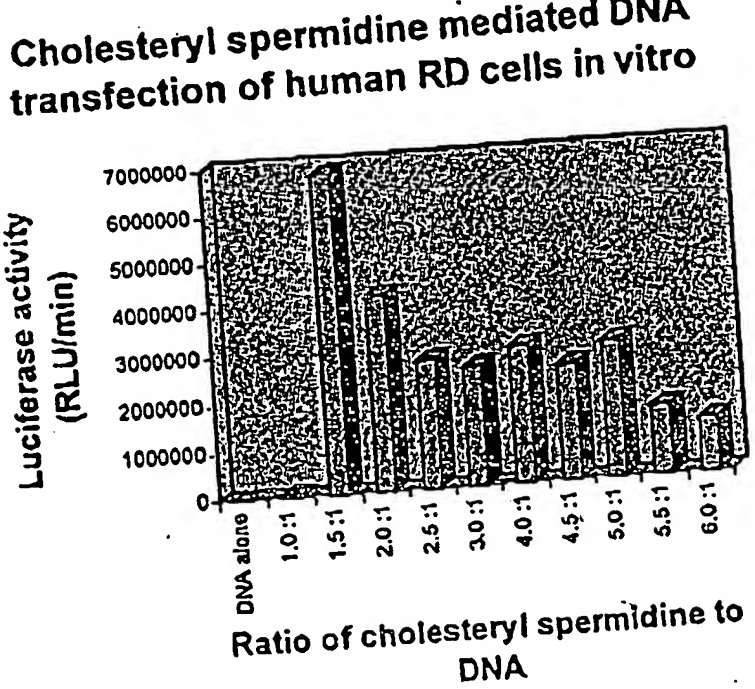

Exhibit 2
Rule 132 Declaration
08/809,397

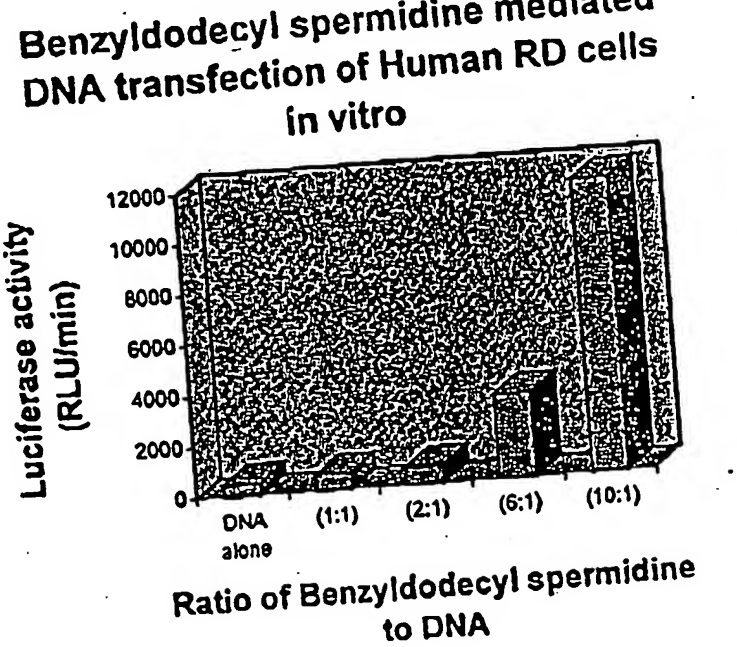

Exhibit 3
Rule 132 Declaration
08/809,397

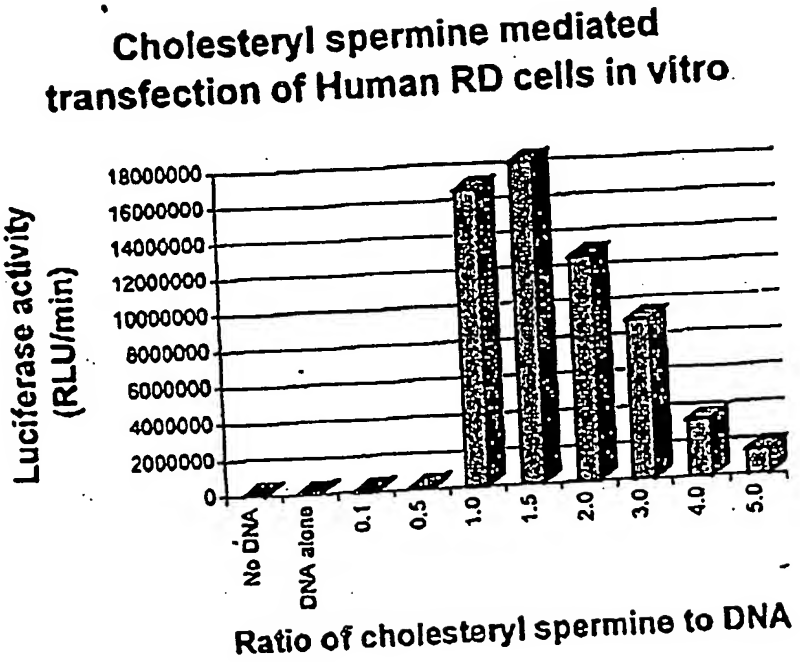

Exhibit 4
Rule 132 Declaration
08/809,397

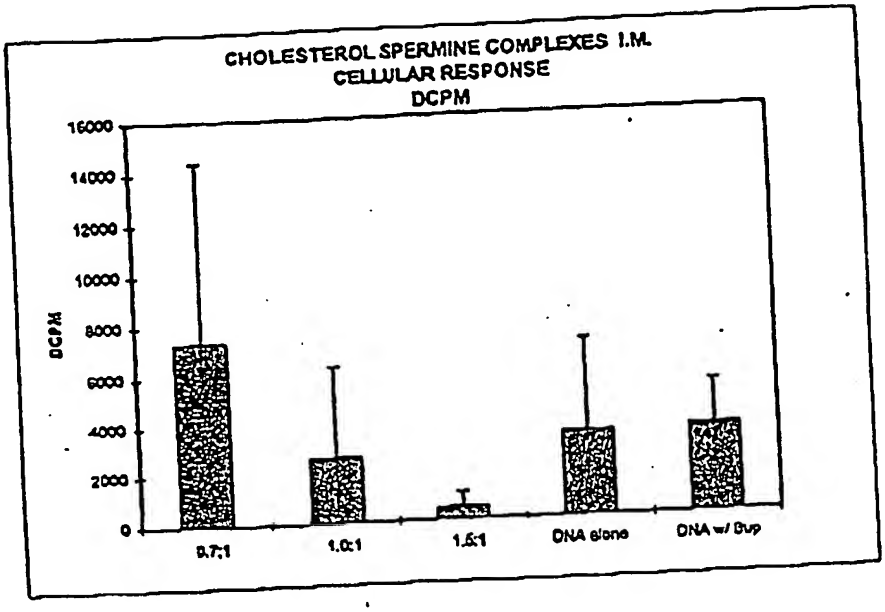

Exhibit 5
Rule 132 Declaration
08/809,397

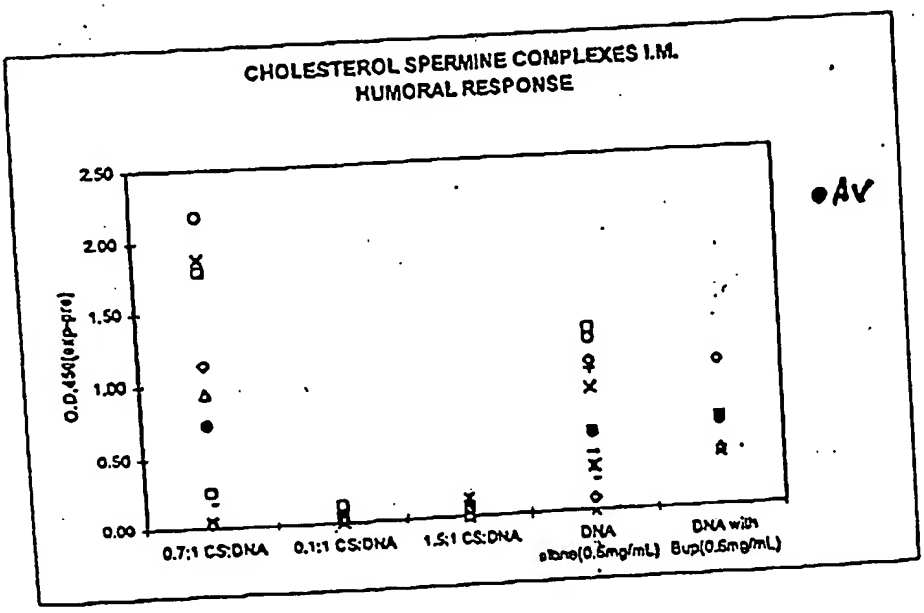

Exhibit 6
Rule 132 Declaration
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JULIA SCHAUER
140 Swinehart Road
Coatesville, Pennsylvania 19320
(610) 383-6358

OBJECTIVE: Pharmaceutical or biotechnology research position which utilizes my pre-medical / chemistry education and extensive experience in organic synthesis, analytical chemistry, protein chemistry, radiochemistry, molecular and cellular biology, and formulations development.

QUALIFIED BY:
* Fourteen years of drug design and vaccine development research experience with increasing responsibilities in project design and management.
* Bachelor of Science in Chemistry plus additional pre-medical course work. (Honors graduate).
* Excellent oral and written communication skills.

"Julia has demonstrated herself to be an excellent communicator and to have the ability to effectively supervise situations and personnel in a matrix structure. We need more employees like this."

Dr. Richard Carrano, Vice President, Technology Devmt. and Regulatory Affairs
1994 Performance Review Excerpts, Apollon, Inc.

EXPERIENCE: **American Home Products, DNA Vaccines Division (formerly Apollon, Inc.), Malvern, PA**

1996-present ***Associate Research Scientist, Molecular and Cellular Biology and Chemistry R&D***
1993-1996 ***Senior Research Associate, Formulations and Chemistry R&D***
1992-1993 ***Research Associate, Chemistry R&D***

My principal duties involved invention and development of novel strategies to deliver gene products to cells. I was involved in all stages of reducing these concepts to practice and testing the resulting product candidates. My areas of technical expertise include:

- *Invention of novel non-viral delivery vehicles for transmembrane passage of DNA.*
  Invented several classes of compounds designed to bind plasmid DNA and exploit both receptor specific and non-specific pathways for uptake into cells. Actively studied the current developments in the field, and lead group discussions at company and team meetings.

- *Design and execution of multistep synthesis of complex organic molecules.*
  Conducted the total synthesis of a variety of molecules including carbohydrates, steroids, peptides, polyamines, and various biomolecules. Thoroughly characterized products by FT NMR (300 MHz), Elemental Analysis, FAB Mass Spectroscopy, HPLC and TLC. Supervised scale up of material for testing, and trained a junior level chemist.

- *Preparation and purification of modified proteins, antibodies and antibody fragments.*
  As the point person in a collaboration with the Molecular Hepatology Dept. at Harvard Medical School, I prepared conjugated IgG antibodies utilizing my own bifunctional ligands. The resulting antibody conjugates were complexed with DNA and tested for receptor targeted cellular uptake in vitro.

- *Development of radioactive assays.*
  Trained with over ten years of experience in handling radioactivity. Prepared and utilized radioactive probes for elucidating DNA complexation mechanisms.

- *Optimization of cultured cell transfection methods for in vitro studies.*
  Conducted cell culture experiments utilizing sterile technique to screen product candidates for efficacy in vitro. Independently optimized the assay and identified the lead compound.

- *Development of formulations methods for evaluation of product stability and efficacy in vivo.*
  Conducted stability studies and physico-chemical characterization of DNA complexes including dynamic light scattering, zeta potential determination, flow cytometric sizing and light microscopy.

1987-1992 **Centocor, Inc., Malvern, PA**

1991-1992 ***Research Associate, Radiochemistry R&D***
1987-1991 ***Senior Research Assistant, Radiochemistry R&D***

- Designed, prepared and tested radioactive imaging agents for cancer and heart disease.
- Prepared and purified modified monoclonal antibody entities as new diagnostic agents.
- Supervised scale up preparation of a new product for use in several human clinical trials.

1984-1986 **Johnson Matthey, Inc., West Chester, PA**

Junior Chemist, Drug Delivery Group, Chemistry R&D

- Conducted organic synthesis of molecules for attachment to platinum as new chemotherapeutic drugs.

EDUCATION: ***West Chester University, West Chester, PA***
Bachelor of Science in Chemistry, 1984.
Cumulative GPA 3.8/4.0. Summa Cum Laude Honors Graduate.

PUBLICATIONS:

Pachuk CJ*, Satishchandran C*, Bayer ME, Samuel M, Zurawski DV, Troutman RD, **Schauer JI** and Ciccarelli RB. *Bupivacaine forms liposomal complexes with DNA.* (in preparation).

L. Mohr, **J.I. Schauer**, R.H. Boutin, D. Moradpour, J.R. Wands. *Targeted gene transfer to hepatocellular carcinoma cells using a novel monoclonal antibody based gene delivery system.* (Manuscript accepted by Hepatology for publication in late 1998).

L. Mohr, **J.I. Schauer**, D. Moradpour, R.H. Boutin, R.B. Ciccarelli, J.R. Wands, and V.R. Zurawski Jr. *Efficient Gene Delivery with Spermidine- and Spermine- Compounds.* Abstract of Papers presented at 1996 Meeting on Gene Therapy, Sept 25-29, 1996, Cold Spring Harbor Laboratory, Cold Spring Harbor, New York.

Darius Moradpour, **Julia I. Schauer**, Vincent R. Zurawski, Jr., Jack R. Wands, and Raymond H. Boutin. *Efficient gene transfer into mammalian cells with cholesteryl-spermidine.* Biochemical and Biophysical Research Communications, 221,82-88 (1996).

Mark A. Nedelman, David J. Shealy, Raymond Boutin, Eva Brunt, **Julia I. Seasholtz** (former name), I. Elaine Allen, John E. McCartney, Frederick D. Warren, Herman Oppermann, Roy H.L. Pang, Harvey J. Berger and Harlan F. Weisman. *Rapid Infarct Imaging with a Technetium-99m-Labeled Antimyosin Recombinant Single-Chain Fv: Evaluation in a Canine Model of Acute Myocardial Infarction.* The Journal of Nuclear Medicine, Vol. 34, No.2, 234-241. (1993).